



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 143552

TO: Zohreh Fay
Location: REM/3C70 *BA61*
Art Unit: 1614
Wednesday, February 02, 2005

Case Serial Number: 09/712612

From: Edward Hart
Location: Biotech-Chem Library
REM-1A55
Phone: 571-272-2512

edward.hart@uspto.gov

Search Notes

Examiner Fay,

Here are the results of the search you requested.

Please feel free to contact me if you have any questions.

Edward Hart

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 15:53:47 ON 02 FEB 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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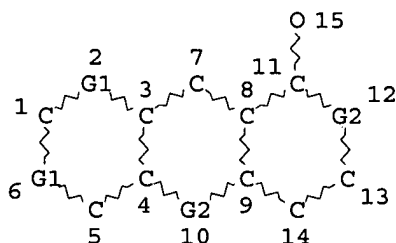
FILE COVERS 1907 - 2 Feb 2005 VOL 142 ISS 6

FILE LAST UPDATED: 1 Feb 2005 (20050201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d stat que

L1 STR



VAR G1=C/N/O/S

VAR G2=N/O/S

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 1

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L3 409 SEA FILE=REGISTRY SSS FUL L1

L4 96 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

L11 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (?CATARACT? OR ?RETIN?)

=> d his

(FILE 'HOME' ENTERED AT 15:24:26 ON 02 FEB 2005)

SET COST OFF

FILE 'REGISTRY' ENTERED AT 15:24:39 ON 02 FEB 2005

L1 STR
 L2 1 S L1
 L3 409 S L2 FULL

FILE 'HCAPLUS' ENTERED AT 15:36:30 ON 02 FEB 2005

L4 96 S L3
 E DIABETES/CT
 L5 10753 S E3
 E E3
 E E3+ALL
 E E2
 E E3
 E E3+ALL
 L6 12538 S E5+OLD
 E DIABETES/CT
 E E12+ALL
 L7 70973 S DIABETES MELLITUS+OLD/CT
 E E20+ALL
 L8 16653 S ANTIDIABETIC AGENTS+OLD/CT
 E US1999-165151/AP,PRN
 L9 1 S L4 AND L5-L8
 E EYE DISEASE/CT
 E E4+ALL
 E E2
 E CATARACT
 L10 7298 S E3-E5
 E CATARACT/CT
 E E3
 E E3+ALL
 L11 0 S L4 AND (?CATARACT? OR ?RETIN?)

FILE 'HCAPLUS' ENTERED AT 15:53:22 ON 02 FEB 2005

FILE 'HCAPLUS' ENTERED AT 15:53:47 ON 02 FEB 2005

=> s ibib abs hitrn l9 tot

MISSING OPERATOR HITRN L9

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> d ibib abs hitrn l9 tot

L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:739571 HCAPLUS

DOCUMENT NUMBER: 137:15586

TITLE: Synthesis and evaluation of novel aldose reductase inhibitors: effects on lens protein kinase Cy

AUTHOR(S): Lewis, S.; Karrer, J.; Saleh, S.; Chen, Y.; Tan, Z.; Hua, D.; McGill, J.; Pang, Y.-P.; Fenwick, B.; Brightman, A.; Takemoto, D.

CORPORATE SOURCE: Department of Biochemistry, Kansas State University, Manhattan, KS, USA

SOURCE: Molecular Vision [online computer file] (2001), 7, 164-171

CODEN: MVEPFB; ISSN: 1090-0535

URL: <http://www.molvis.org/molvis/v7/a23/lewis.pdf>

PUBLISHER: Molecular Vision

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB The aim of the study was to synthesize novel aldose reductase inhibitors

(ARI) that will normalize losses in protein kinase Cy (PKCy) observed during diabetes and galactosemia. ARI were synthesized as tricyclic pyrones (HAR-1 through HAR-6) from 3-methyl-1H,7H-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-b][1]benzopyran and (5aS,7S)-7-isopropenyl-3-methyl-1H,7H-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-b][1]benzopyran and were tested by inhibition of aldose reductase enzyme activity in vitro and by inhibition of polyol formation in lens epithelial cells in culture. Identified compds. were further tested in galactosemic rat lens in vivo for (a) normalized PKCy levels by Western blot, (b) reduction of phosphorylation of the gap junction protein Cx46 by analyses of co-immunopptd. proteins, and (c) by normalization of gap junction activity as measured by dye transfer. HAR-1 (1H,7H-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-b][1]benzopyran-3-acetic acid) was identified as an ARI with IC50 for aldose reductase inhibition at 2 nM. Polyol accumulation in lens epithelial cells was reduced by 80% at 10 μ M. Rats fed 40% galactose for 9 days had an 80% reduction in PKCy levels which were normalized by HAR-1 at 100 mg/kg/day, fed orally. Phosphorylation of Cx46 was increased by 50% and this was normalized in HAR-1 treated rats (6 day treatment). Gap junction activity of galactosemic rats was reduced by 55% and this was normalized by HAR-1 in six day-treated rats. HAR-1 is a novel ARI which normalized losses of PKCy, changes in Cx46 phosphorylation, and gap junction activity.

IT 434954-53-7P 434954-54-8P 434954-55-9P
434954-56-0P 434954-57-1P 435269-05-9P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and evaluation of novel aldose reductase inhibitors)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> sel hit rn 19

E1 THROUGH E6 ASSIGNED

=> file reg

FILE 'REGISTRY' ENTERED AT 15:54:49 ON 02 FEB 2005

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 FEB 2005 HIGHEST RN 824390-04-7

DICTIONARY FILE UPDATES: 1 FEB 2005 HIGHEST RN 824390-04-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s el-e6

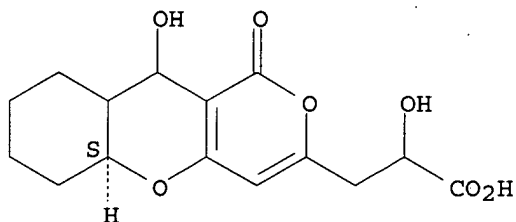
1 434954-53-7/BI
 (434954-53-7/RN)
 1 434954-54-8/BI
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 (434954-55-9/RN)
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 (434954-57-1/RN)
 1 435269-05-9/BI
 (435269-05-9/RN)

L12 6 (434954-53-7/BI OR 434954-54-8/BI OR 434954-55-9/BI OR 434954-56-0/BI OR 434954-57-1/BI OR 435269-05-9/BI)

=> d ide can l12 tot

L12 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 435269-05-9 REGISTRY
 CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-propanoic acid, 5a,6,8,9,9a,10-hexahydro- α ,10-dihydroxy-1-oxo-, (5aS)-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C15 H18 O7
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

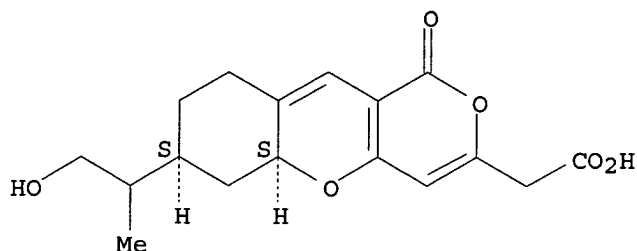
1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:15586

L12 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 434954-57-1 REGISTRY
 CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-acetic acid, 5a,6,8,9-tetrahydro-7-(2-hydroxy-1-methylethyl)-1-oxo-, (5aS,7S)-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C17 H20 O6
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);

USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:15586

L12 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 434954-56-0 REGISTRY

CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-acetic acid, 5a,6,8,9-tetrahydro-7-(1-methylethenyl)-1-oxo-, (5aS,7S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C17 H18 O5

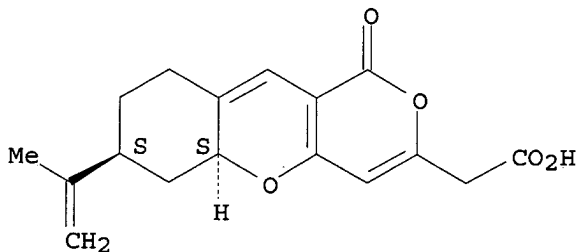
SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:261078

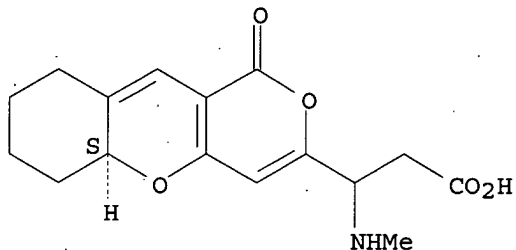
REFERENCE 2: 137:15586

L12 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 434954-55-9 REGISTRY

CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-propanoic acid, 5a,6,8,9-tetrahydro-
 β -(methylamino)-1-oxo-, (5aS)-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C16 H19 N O5
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 USES (Uses)

Absolute stereochemistry.



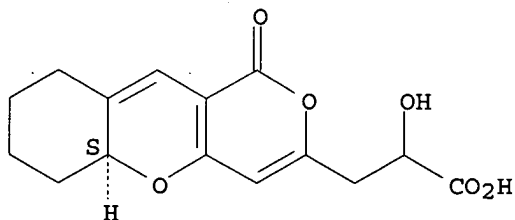
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:15586

L12 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 434954-54-8 REGISTRY
 CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-propanoic acid, 5a,6,8,9-tetrahydro-
 α -hydroxy-1-oxo-, (5aS)-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C15 H16 O6
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 USES (Uses)

Absolute stereochemistry.



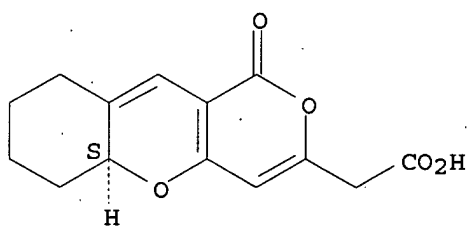
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:15586

L12 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
RN 434954-53-7 REGISTRY
CN 1H,7H-Pyrano[4,3-b][1]benzopyran-3-acetic acid, 5a,6,8,9-tetrahydro-1-oxo-, (5aS)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H14 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:388584

REFERENCE 2: 137:15586